National Institute of Allergy and Infectious Diseases
National Institutes of Health

Division of AIDS **revised April 11, 2005**

Supplemental Questions and Answers

Leadership for HIV/AIDS Clinical Trials Networks

Research Plan

1. As the Networks are currently being restructured and there will likely be a new Microbicide network, what is the expected relationship between the existing HPTN and the proposed microbicide network? How should a microbicide-focused Clinical Trials Unit compete under the new RFA?

An applicant for a Clinical Trials Unit (CTU) may propose affiliation with more than one Clinical Trials Network. However, until applications are actually received, it is impossible to know what the relationship is between the current HPTN and a Network Leadership applicant focused on microbicide research. The CTU and/or site Principal Investigator is/are expected, and encouraged, to contact the leadership of existing Networks and/or potential future Networks in order to identify the best fit with respect to the Network's research plans and the CTU's expertise and capabilities.

NIAID has made available a Web site designed to facilitate information sharing between applicants to the "Leadership for HIV/AIDS Clinical Trials Networks" and "Units for HIV/AIDS Clinical Trials Networks." Applicants may, at their choosing, use this Web site to share information about applicant Network clinical research plans and Network capacity needs, as well as the interests and availability of Clinical Trials Units and Clinical Research Sites. NIAID will accept and post information, statements of interest, and contact information. Instructions for submitting information for posting are available at http://www.niaid.nih.gov/daids/rfa/network06. All postings will remain on the Web site until the final receipt date for applications.

Based on the available information and additional discussions with applicants for the Network Leadership, the Principal Investigator of each CTU application will then decide which Clinical Trials Networks are best aligned with the CTU's expertise and capabilities.

2. How can applicants for Clinical Trials Units and Clinical Research Sites contact applicants for Network Leadership for consideration in their Leadership applications?

As noted above (see question #1), NIAID has made available a Web site designed to facilitate information sharing between Network Leadership and Clinical Trials Units applicants. While it is strongly recommended that applicants use this resource to communicate about potential affiliations, please note that since use of this site is voluntary, NIAID cannot require applicants to share this information nor should this Web site be considered to be a complete listing of potential applicants. In addition, it is expected that communication between prospective Network Leadership and Clinical Trials Units will occur through the scientific research community.

3. Would it be suitable under a Network Leadership application to organize a central laboratory to handle CD4 T cell counts and/or to handle routine monitoring of safety labs such as chemistries and CBCs?

Investigators are encouraged to propose central testing for assays that are not adversely affected by the shipping of samples, when timeframes for reporting of results are such that participant safety is not adversely impacted, and when centralization results in reliable, reproducible data sets and cost savings.

Application Options, Application Assembly and Page Limits

1. Is a letter of intent required?

A letter of intent is not required or binding, and does not affect the review of a subsequent application. NIAID staff use the information in a letter of intent to estimate peer review workload and begin planning for a review.

2. What is the due date for Network Leadership applications?

The Center for Scientific Review must receive a signed, typewritten original of the application, including the checklist, and three signed photocopies in one package by commercial carrier by May 11, 2005. At the same time, send two exact copies of the application and all five sets of any appendix materials to the peer review staff listed in the RFA.

3. How are the applications to be delivered to the NIH?

The application submission requirements are detailed in Section IV of the RFA. The actual delivery can only be accomplished by a courier service such as the U.S. Postal Service, Federal Express, United Parcel Service (UPS), DHL, or similar service. Hand delivery of materials by applicants is not permitted

4. Please provide some clarification on the process of transitioning clinical research activities and components.

It is recommended that applicants complete "Leadership Table 4," available at http://www.niaid.nih.gov/daids/rfa/network06, to summarize transitional activities and components.

Applicants requesting funding for incumbent Networks or for new Networks that will include clinical research activities that are ongoing at the time of award must identify each protocol, its status, the anticipated time and approximate costs for completion. These costs should include outlays at the Clinical Research Sites and be based on formula(s) developed for the Protocol Implementation Fund. These costs for year 1 only should be included in the Network CORE budget in the section "Other Expenses" budget category identified as "Transition Costs."

Applicants must also identify existing clinical trials infrastructure, such as Clinical Research Sites, laboratories, operations offices, data management centers and clinical trial materials (e.g., specimens and completed case report forms) that will require phase-out. Applicants must also propose a phase-out schedule and budget. While it is not needed at this time, DAIDS may eventually request a list of accurate and updated information such as specimen and reagent inventories, data files, original data and any necessary related information, labeled and inventoried paper files, a list of government-owned equipment and property, etc.

Network Leadership applicants must identify Clinical Research Sites that are slated for discontinuation and propose milestones and a timeline for development and a phase-out budget.

5. Is a progress report expected (as is the case with most competing renewal applications)?

These are not competing renewal applications. As a result, a progress report for work to date is not expected at this time. Information regarding ongoing studies will be obtained through the tables requested under the transition section of the RFA and any final reports that are submitted as per the requirements of the existing grant.

Please note that although a progress report is not needed at this time, if an award is made, a progress report will be required as a condition of continued funding in the future. A final report will also be required.

6. Where in the application should a list of publications from the current funding period be included, and is this listing excluded from the page limitations, as is true for other grant applications?

The list should be part of the Biographical Sketch, which is excluded from the page limitations. As this is not a competing renewal application, please follow the PHS 398 instructions on publications.

7. Can I submit my application on A4 paper?

The NIH Center for Scientific Review (CSR) has determined that applicants may submit on A4 paper, as long as the printed area does not exceed the area of a standard PHS 398 form page (8.5 x 11 inches, less margins) since CSR must scan and duplicate each application onto 8.5 x 11 inch paper. A4 sheets should be printed with a 1-inch top margin, 5/8 inch left margin, 1/2-inch right margin, and 1-3/8 inch bottom margin. The printed area (including page number) should extend no more than 10 1/2 inches from the top of the page. Applicants must ensure that application documents satisfy all other CSR format requirements, such as minimum font size, minimum line spacing, etc.

Clinical Trials Units

1. How will patients co-enrolled in multiple protocols be counted?

Patients will be counted toward every study in which they participate. However, for the purpose of satisfying the Clinical Research Site Core Capacity requirement (an average of 20 participants per month on-study), only those patients enrolled in main studies will be counted. For example, if a patient is co-enrolled in two main studies, that patient would be counted twice. However, if a patient is enrolled in one main study and one substudy, they would only be counted once. Patients who are co-enrolled in substudies would be acknowledged (counted) for the purpose of site performance evaluations and budgeting, but not toward meeting the minimum capacity requirement.

For purposes of determining core capacity at Clinical Research Sites, enrollment pairs, e.g., mother-infant pairs, serodiscordant couples, may be counted as individual participants depending on how the protocol is described. However, for the purpose of determining CTU core costs, each enrollment pair should be counted as one participant.

Laboratory Questions

NOTE: For full details on the answers to questions 1-4 please refer to the RFA: Part II → Section IV → Item 6 → Item V → Item D → Item 3.

1. What will DAIDS require from the central laboratories in terms of validated assays and GLP-compliance?

Network laboratories, including those outside the United States, are required to be GLP-compliant and use validated assays.

2. If an applicant chooses to use a contract lab, will that lab be required to participate in the DAIDS Virology Quality Assurance (VQA) program?

Yes, all labs performing viral loads as an endpoint are required to participate in the DAIDS VQA program.

3. Is a master list of SOPs acceptable for the research plan, or are applicants required to submit the actual SOPs for what is listed?

A master list of SOPs is acceptable. However, the actual SOPs may be requested at a future date.

4. Should training SOPs be limited to specimen handling, processing, etc. or should applicants include training plans for laboratory-specific assays (e.g., endpoint assays, safety) as well?

All aspects of training laboratory staff to perform required lab functions (e.g., all laboratory assays, specimen handling, processing, tracking, the Laboratory Data Management System, etc.), as well as an overall training plan for safety training, should be documented in training SOPs. These SOPs should be included on the master list of SOPs.

5. How will other DAIDS laboratory support contracts (Immunology Quality Assurance, VQA, and Safety Monitoring in International Laboratories [SMILE]) be used in relationship to the new Leadership NLS? How will the Network laboratories access these services?

The Immunology Quality Assessment (IQA), Virology Quality Assessment (VQA), and Safety Monitoring in International Laboratories (SMILE) are contractual resources that DAIDS uses to evaluate and develop the capability of laboratories to participate in DAIDS-supported clinical studies. The NLS will be required to enroll their laboratories in these programs.

6. What are DAIDS' requirements for different types of Network laboratories, such as safety labs or labs performing endpoint analyses?

Safety laboratories in the United States must be CLIA-accredited and participate in CAP proficiency testing schemes. HIV diagnosis must include ELISA and confirmation by Western Blot (WB). Labs performing CD4 counts, viral load and/or HIV resistance testing for patient management must participate in the IQA and VQA programs, respectively.

International Safety Laboratories must participate in external proficiency testing for all safety tests specified in the clinical study protocol. For HIV diagnosis, FDA-approved rapid tests may be used for screening only; a positive result must be confirmed by WB or parallel testing by two different rapid tests that have been compared to a "gold standard" and show comparable performance.

All laboratory endpoint testing must be performed using validated assays in a GLP-compliant environment. Those laboratories must also participate in VQA and/or IQA programs.

If a Network laboratory utilizes a contract laboratory for viral load testing or endpoint determination, the contract laboratory must be enrolled in the VQA and/or IQA program.

7. Can Networks establish specimen repositories to control how specimens are stored, tracked and managed, in order to maintain the quality of the process?

DAIDS would encourage the Network Laboratory Structure to use existing resources such as the DAIDS Reference and Reagent Repository and/or the DAIDS Specimen Repository. However, if a Network Laboratory Structure chooses to establish and fund its own Repository, the Repository would be subject to performing specimen management utilizing GLP and establishing a Laboratory Data Management System to track and manage specimens. This latter system should be compliant with FDA regulations and would be subject to external GLP audits.